## REMARKS

The present response is intended to be fully responsive to all points of objection and/or rejection raised by the Examiner and is believed to place the application in condition for allowance. In order to expedite prosecution, Applicants are submitting herewith a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, together with new claims 48-61. Favorable reconsideration and allowance of new claims 48-61 under 37 C.F.R. § 1.114 is respectfully requested.

### Status of Claims

Claims 1-18, 20-28, and 42-47 are pending in the application. Claims 24, 25, and 42-47 have been withdrawn from consideration by the Examiner. Claims 1-18, 20-23, and 26-28 have been rejected.

Claims 1-18, 20-23, and 26-28 are herein cancelled, and new claims 48-61 added. New claims contain no new matter. Therefore, Applicants respectfully request entry of the Amendment.

## OBJECTIONS TO THE SPECIFICATION

In the August 25, 2004 Office Action, the Examiner maintained the objection to the specification made in paragraph 5(iv) of the January 8, 2004 Office Action, asserting that "The amended Figure 1 submitted 05/10/04 does not depict any part of the structure in 'bold.'"

Applicants traverse the Examiner's objection. Applicants amended the subject specification (page 4, third paragraph of the May 10, 2004 Amendment), replacing the phrase "indicated in boldface" with the word "underlined." Accordingly, Figure 1 is consistent with the reference thereto in the specification, and Applicants respectfully request that the Examiner withdraw the objection.

## CLAIM REJECTIONS-35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner further maintained the rejection of claim 14 made in the January 8, 2004 Office Action under 35 U.S.C. § 112, first paragraph, citing lack of a statement by an attorney of record stating that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on the application.

In response, Applicants hereby certify that all restrictions upon public access to the deposit IDAC 260900-1 will be irrevocably removed upon the grant of a patent on the subject application, in accordance with the requirements of 37 CFR § 1.808. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

The Examiner has rejected claims 1-18, 20-23, and 26-28 under 35 U.S.C. § 112, first paragraph, for allegedly containing new subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. Specifically, the Examiner objected to the allegedly new limitations "structural equivalent thereof" (claims 9-10), "a lipopolysaccharide outer core of a bacterial capsule" (claim 20), "further comprising a second immunogenic component, said second immunogenic component being an epitope on a *Neisseria* lipopolysaccharide inner core... wherein said phosphoethanolamine moiety of said second immunogenic component is linked to a different position of said HepII of the inner core than said phosphoethanolamine moiety of the immunogenic component of claim 1" (claim 15), "wherein said immunogenic... has two phosphoethanolamine moieties located at two positions on said HepII, a first said position being the 3- position, and a second said position being the 6- or the 7- position" (claim 16), "wherein said immunogenic element is capable of stimulating antibodies which are opsonic for pathogenic *Neisseria*" (claim 21), "a condition characterized by *Neisseria* infection" (claims 22-23), and "wherein said commensal *Neisseria* is *Neisseria lactamica*" (claim 28)

In addition, the Examiner objected to the limitations "wherein the vaccine is capable of eliciting protective and/or immunoprophylactic antibodies against a pathogenic *Neisseria* strain" (claims 1 and 14), "protective and/or immunoprophylactic antibodies against... pathogenic *Neisseria* strain" (claims 2 and 3), "wherein said vaccine elicits protective and/or

immunoprophylactic antibodies against at least...% of pathogenic *Neisseria* strains" (claims 17-18), and "the antibodies are elicited by... an immunogenic component of at least...% of group B strains of *Neisseria* meningitidis" (claims 6-8).

In response, in order to expedite prosecution, new claims 48-61 are directed to (a) methods for eliciting in a host an antibody that recognizes a plurality of *Neisseria* immunotypes, comprising administering to the host an immunogenic composition comprising a *Neisseria* LPS inner core, wherein a phosphatidylethanolamine (hereinafter referred to as "PEA") moiety is linked to position 3 of a HepII moiety of the inner core; and (b) methods of immunizing a host against each of a plurality of *Neisseria* immunotypes, comprising same. The new claims do not contain any of the objected-to limitations or objected-to allegedly new matter.

Support for new claims 48 and 50-53 is found, *inter alia*, page 31, second full paragraph. As stated therein, the subject application demonstrates that (a) the presence of PEA at position 3 of HepII of the inner core oligosaccharide (OS) defines an antibody epitope, i.e. the epitope recognized by MAb B5; and (b) the epitope is present on *Neisseria* immunotypes L1, L3, and each of L7-12. These findings would unquestionably show a person of average skill in the art that the immunogenic composition recited in the new claims elicits an antibody that recognizes the eight named *Neisseria* immunotypes, as claimed in claims 48 and 50-53. Support for new claims 55 and 57-60 is found in the above passages, together with the findings that that antibodies to the epitope are opsonic and bactericidal and passively protect subjects against *Neisseria meningitidis* infection (pages 56-58). Support for new dependent claims 54 and 61 is found in the third full paragraph of page 31. Support for new dependent claims 49 and 56 is found in Figure 1.

Since the new claims do not contain any of the limitations objected to by the Examiner, and the new claims are supported by the subject specification, Applicants respectfully request that the Examiner withdraw the rejections.

## CLAIM REJECTIONS-35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has further rejected claims 1-18, 20-23, and 26-28 under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention (pages 13-16 of the Office Action).

In response, in order to expedite prosecution, new claims 48-61 have been filed. The new claims do not contain any of the objected-to alleged ambiguities.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejections.

## PRIORITY REJECTIONS

In the August 25, 2004 Office Action, the Examiner rejected Applicants' claim to priority from U.S. Provisional Applications 60/196,305, filed 4/12/00 and 60/156,940, filed 09/30/99, alleging

> "The ***vaccine as claimed that is capable of eliciting protective and/or immunoprophylactic antibodies against the recited pathogenic Neisseria strain*** is not enabled or described in the provisional application... instant claims are not granted priority to 9/30/99 ***because of new matter contained in the claims, as amended***" (paragraph beginning on page 7).

The Examiner admitted, however, that U.S. Provisional Application 60/156,940, filed 09/30/99, is enabling for

> "an immunogenic composition... which on active immunization elicits antibodies reactive with the LPS inner core of said *galE* mutant and a Neisserial inner core LPS epitope containing phosphatidylethanolamine at position 3 of HepII" (January 8, 2004 Office Action, page 5, second full paragraph).

In response, the new claims are directed to (a) methods for eliciting in a host an antibody that recognizes a plurality of *Neisseria* immunotypes, comprising administering to the host an immunogenic composition comprising a *Neisseria* LPS inner core, wherein a PEA

moiety is linked to position 3 of a HepII moiety of the inner core; and (b) methods of immunizing a host against each of a plurality of *Neisseria* immunotypes, comprising same. The new claims do not contain the objected-to limitation "vaccine...that is capable of eliciting protective and/or immunoprophylactic antibodies against the recited pathogenic Neisseria strain." In addition, the new claims do not contain the objected-to allegedly new matter, as described above in the section addressing the claim rejections under 35 U.S.C. § 112, first paragraph.

Support for new independent claim 48 and new dependent claims 50-53 is found in the first full paragraph of page 16 of U.S. Provisional Application 60/156,940, which corresponds to the second full paragraph of page 31, described above in the section addressing the claim rejections under 35 U.S.C. § 112, first paragraph. Support for new independent claim 55 and new dependent claims 57-60 is found in the above passage in combination with page 21 of U.S. Provisional Application 60/156,940, which states "mAb B5 is opsonic in the presence of complement and that the uptake of *Nm* bacteria correlates with an oxidative burst reaction within the neutrophil;" exactly the same sentence in the Plested reference was used by the Examiner to show that the vaccine disclosed in Plested was sufficiently enabled to allegedly anticipate claims of the subject application directed vaccines for the treatment of disease caused by pathogenic *Neisseria* (January 8, 2004 Office Action; page 17, lines 23-24). Support for new dependent claims 54 and 61 is found in the first full paragraph of page 18 of U.S. Provisional Application 60/156,940, which describes the *Neisseria* strains as "*Nm*" (*Neisseria meningitidis*). Support for new dependent claims 49 and 56 is found in Figure 1 of U.S. Provisional Application 60/156,940. In addition, U.S. Provisional Application 60/196,305 further elaborates upon the findings of Provisional Application 60/156,940.

Since the new claims do not contain the allegedly new matter and are clearly supported by U.S. Provisional Applications 60/196,305 and 60/156,940, Applicants respectfully request that the Examiner withdraw the rejection and grant claims of the subject application a priority of U.S. Provisional Applications 60/196,305 and 60/156,940.

## CLAIM REJECTIONS- 35 U.S.C. § 102

The Examiner maintained the rejection made in the January 8, 2004 Office Action of claims 1-18 and 20-23 under 35 U.S.C. § 102(b) as being anticipated by Plested et al, alleging that "Plested et al is properly applied under 35 U.S.C. § 102 since instant claims are not granted priority to 9/30/99 because of new matter contained in the claims, as amended."

Applicants respectfully disagree. Applicants assert that the subject matter defined by new claims 48-61 is entitled to a priority date of 9/30/99, the filing date of U.S. Provisional Application 60/156,940, as the subject matter is are fully described and enabled therein, as described above, and thus properly claims priority therefrom. Since the 9/30/99 filing date of Provisional Application 60/156,940 precedes the October 1999 publication date of Plested, Plested et al is not an appropriate 35 U.S.C. § 102 reference, and Applicants respectfully request withdrawal of the rejection.

The Examiner further maintained the rejection made in the January 8, 2004 Office Action of claims 1-12, 14-18, 20-22, and 26 under 35 U.S.C. § 102(b) as being anticipated by Verheul et al as evidenced by Plested et al. The Examiner alleged that Verheul discloses a vaccine "comprising at least one immunogenic component, the immunogenic component being an epitope on a Neisseria lipopolysaccharide inner core characterized by the presence of a phosphoethanolamine moiety linked to a 3, 6, 7, or a combination thereof, position of HepII of the inner core," as claimed in the subject claims. The Examiner alleged that use of the open-ended terms "comprising," "characterized by," and "at least" in the subject claims caused the compositions disclosed by Verheul to fall within the scope of the subject claims. The Examiner admitted, however, that Verheul did not show that the antibodies elicited are specific to PEA at the 3-position of HepII and are opsonically functional, rather using Plested et al to show same (page 10, first full paragraph of the August 25, 2004 Office Action).

In response, Applicants respectfully traverse the rejection and agree that Verheul did not disclose antibodies specific to PEA at the 3-position of HepII. New claims 48-61 are directed to (a) methods for eliciting in a host an antibody that recognizes a plurality of *Neisseria* immunotypes, comprising administering to the host an immunogenic composition comprising a *Neisseria* LPS inner core, wherein a PEA moiety is linked to position 3 of a

HepII moiety of the inner core; and (b) methods of immunizing a host against each of a plurality of *Neisseria* immunotypes, comprising same. The subject application shows that the presence of PEA at position 3 of HepII of the inner core OS defines an antibody epitope and that the epitope is present on multiple *Neisseria* immunotypes, via (a) use of a galE *Neisseria* mutant in which the outer core of the LPS is not present, thus genetically separating inner core and outer core epitopes; and (b) extensive chemical and genetic experimentation, further characterizing the epitope. In view of these findings, a person of average skill in the art would accept the subject application as credible evidence that administration of the recited epitope would elicit in a host an antibody that recognizes a plurality of *Neisseria* immunotypes, as claimed in claims 48-54 of the subject application.

In sharp contrast, Verheul did not perform any experiments to define an epitope that exhibits cross-reactivity among different *Neisseria* immunotypes. In addition, Verheul utilized immunogenic compositions that would be expected by a person of average skill in the art to elicit a large percentage of antibodies irrelevant to *Neisseria* inner core epitopes. In these compositions, (a) the LPS is conjugated to a carrier protein (abstract); (b) only the lipid A fraction of the LPS was removed, the entire remainder of the molecule, including the outer core, being conjugated to the peptide, as shown in Figure 1 (page 844); (c) the Kdo moiety is modified (page 844, first full paragraph); and (d) 15-mers, as opposed to monomers, of the OS are present in the conjugates (Table 3, page 847). In addition, the authors of Verheul themselves admitted that the OS in the OS-protein conjugates they utilized was not homogenous, and that the monosaccharide composition of the OS was altered by conjugation (paragraph beginning on page 847; first full paragraph on page 848). Thus, the compositions utilized by Verheul to generate antibodies had very different characteristics than naturally occurring LPS molecules. As a result, a large percentage of the antibodies generated using these compositions were not directed to inner core OS epitopes, as evidenced by Verheul's finding that the amount of whole LPS required to neutralize the antisera was a small fraction of the amount of OS required (Table 4, page 850).

Moreover, Verheul did not conduct studies to determine the structure of the molecules used to generate antibodies, and thus ***did not know their structure***. In the absence of any structural determination by Verheul, a person of average skill in the art would not have taken

Verheul as credible evidence for an antibody epitope defined by the presence of PEA at position 3 of HepII of the inner core OS, as recited in new claims of the subject application. The Examiner admitted this point in the August 25, 2004 Office Action, in which the Examiner stated that the Plested reference is necessary to show the presence of the above epitope (page 10, first full paragraph). As described above, Plested et al is not an appropriate 35 U.S.C. § 102 reference for the subject application, and therefore should not be used to show inherent properties of the vaccine disclosed in Verheul for purposes of a 35 U.S.C. § 102 rejection. The most that could have been concluded from Verheul by a person of average skill in the art was that "Antisera evoked with a PEA-containing conjugate... ***probably contain*** antibodies directed against ***PEA-group containing epitopes***" (page 850, first full paragraph). Verheul, with their lack of certainty as to the presence and amount, if present, of antibodies against PEA-containing epitopes, and total lack of knowledge as to the structure of the epitope, clearly failed to disclose or suggest the cross-reactive epitope recited in new claims 48-54 of the subject application.

The Examiner further alleged (page 10, first full paragraph of the August 25, 2004 Office Action) that Verheul taught that "LPS alone and LPS conjugates elicited specific IgG responses (see Figure 3 and page 848)."

Applicants respectfully disagree. This finding is irrelevant to the methods recited in the new claims, since (a) the epitope specificity of the responses; (b) and the ability of the antisera induced to recognize multiple *Neisseria* immunotypes were not ascertained. In addition, an examination of Figure 3 of Verheul teaches away from the conclusion that antibodies were elicited to unconjugated LPS. The error bars of the responses to unconjugated LPS are larger than the responses themselves, which would have caused a person of average skill in the art to seriously question the statistical significance of the responses. Thus, Figure 3 of Verheul neither disclosed nor suggested the invention claimed in the subject application.

The Examiner further alleged (page 10, first full paragraph) that Verheul taught that whole cell *meningoccal* bacteria elicited antibodies against PEA-containing epitopes.

Applicants respectfully disagree. This alleged finding did not in any way show the presence of the epitope recited in the new claims of the subject application. In addition, Verheul did not test for cross-reactivity of the antisera against multiple strains. Thus, Verheul neither disclosed nor suggested the epitope claimed in the subject application or methods comprising same.

The Examiner further alleged (page 10, first full paragraph) that the subject specification attributed to Verheul the finding that the presence of PEA in the 3-position of HepII defines an immunological epitope. In fact, Verheul showed nothing of the sort, as described above. Applicants declare that the attribution of this finding to Verheul in the subject specification was a mistake.

Since the *Neisserial* inner core LPS epitope containing PEA at position 3 of HepII, as recited in the new claims of the subject application, was not disclosed by Verheul, and since Plested is not an appropriate reference for showing inherent properties an alleged prior art composition for purposes of a 35 U.S.C. § 102 rejection, the 35 U.S.C. § 102 rejection of new claims 48-54 in view of Verheul as evidenced by Plested is incorrect.

Accordingly, Applicants respectfully request that the Examiner allow claims 48-54 of the subject application.

Furthermore, Verheul did not show that the antibody epitope recited in the claims of the subject application is useful for vaccination against each of a plurality of *Neisseria* immunotypes, as recited in new claims 55-61 of the subject application, directed to methods of immunizing a host against each of a plurality of *Neisseria* immunotypes, comprising administering to the host an immunogenic composition comprising a *Neisseria* LPS inner core, wherein a PEA moiety is linked to position 3 of a HepII moiety of the inner core. By contrast, the subject application showed that the epitope recited in the claims was present and accessible on 70% of the most complete set of invasive *Neisseria* lineages known (page 33, first full paragraph); and that antibodies elicited by the recited epitope are opsonic and bactericidal and passively protect subjects against *Neisseria meningitidis* infection (pages 56-58). By contrast, none of this was shown by Verheul; in fact, as stated by the Examiner in the August 25, 2004 Office Action (page 10, first full paragraph), the Plested reference was

required to show that the antibodies elicited by Verheul's compositions were opsonically functional.

Thus, the subject application, but not Verheul, provides a credible expectation to a person of average skill in the art that the presence of the epitope recited in the claims would render a composition useful in vaccination against each of a plurality of *Neisseria* immunotypes. Since Verheul did not disclose the utility of the above epitope in vaccination against *Neisseria*, and since Plested is not an appropriate reference for showing inherent properties of an alleged prior art composition for purposes of a 35 U.S.C. § 102 rejection, the 35 U.S.C. § 102 rejection of new claims 55-61 in view of Verheul as evidenced by Plested is incorrect.

Accordingly, Applicants respectfully request that the Examiner withdraw the 35 U.S.C. § 102 rejection of the claims of the subject application in view of Verheul.

The Examiner has further rejected claims 1-18, 20-23, and 26-27 under 35 U.S.C. § 102(b) as being anticipated by Hoogerhout et al as evidenced by Goldschneider et al. The Examiner alleged that Hoogerhout disclosed (1) a vaccine composition containing at least one epitope that imparted cross-reactive immunity against one, two, or more immunotypes of meningococcus including L1, L2, and L3; (2) that the vaccine composition contains the meningococcal LPS OS core region and a conjugate thereof; (3) that the basic core structure depicted contains PEA groups; (4) that a preferred saccharide-peptide conjugate containing a PEA-containing part may exhibit cross-reactivity with multiple bacterial immunotypes, e.g. L2 and L3 or L1 and L3; (5) that immunotypes L3 and L2 cause approximately 70% to 30% of group B meningococcal meningitidis; and (6) that the PEA group of bacterial inner core LPS forms a number of immunotype-specific epitopes. Goldschneider was used by the Examiner to allegedly show that *N. meningitidis* is a commensal species.

Applicants respectfully disagree. Contrary to the Examiner's assertion, Hoogerhout does not disclose any vaccine compositions containing only the *Neisserial* LPS epitope; rather, the LPS in all the disclosed compositions is conjugated to peptides. The exclusive use of LPS-peptide conjugates by Hoogerhout in fact teaches away from the (a) methods for eliciting in a host an antibody that recognizes a plurality of *Neisseria* immunotypes; and (b) methods of immunizing a host against each of a plurality of *Neisseria* immunotypes,

comprising administering to the host an immunogenic composition comprising a *Neisseria* LPS inner core, wherein a PEA moiety is linked to position 3 of a HepII moiety of the inner core, as recited in the new claims of the subject application. Because the vaccine compositions of Hoogerhout are all conjugated to peptides, they contain many antibody epitopes irrelevant to the antibody epitope of the subject application, and thus would be expected by a person of average skill in the art to elicit many antibodies irrelevant to the antibody epitope of the subject application, as shown above in the case of Verheul.

Other statements by Hoogerhout also serve to teach away from the epitope recited in the claims of the subject application, which is defined by the location of the PEA group. Hoogerhout states:

> "The oligosaccharides of the immunotypes differ with regard to the monosaccharide composition, quantity and location of PEA groups and the degrees of acetylation of the α (1→2)-bound GlcNAc unit or other units. The basic structure of the oligosaccharide 'core' is similar for most immunotypes" (page 7, fourth full paragraph).

Thus, Hoogerhout enumerates three differences between inner core immunotypes, without indicating which difference, if any, is the most important. According to Hoogerhout, any of these differences might determine immunoreactivity of a particular immunotype. Therefore, Hoogerhout demonstrates lack of knowledge of the cross-reactive epitope recited in the new claims of the subject application, which is defined solely by the location of the PEA group.

The Examiner further alleged that Hoogerhout disclosed "a conjugate...that imparted cross-reactive immunity against one, two, or more immunotypes of *meningococcus* including L1, L2, and L3" and "one or more saccharide core epitopes of more than one epitope which elicits immunity specific for one immunotype or more than one immunotype" (bridging page 16 and page 17). Examination of the quoted passages reveals that (a) Hoogerhout was not certain of the presence of the cross-reactive epitope; and (b) the cross-reactive epitope referred to is different from the epitope recited in claims of the subject application:

> "Futhermore, there is also a ***possibility*** for the synthesis of a saccharide part containing a minimal oligosaccharide with activity that imparts cross-reactive immunity" (paragraph bridging pages 18 and 19).
>
> "Saccharide-peptide conjugate according to claim 29, characterized by the fact that the conjugate ***shows cross reaction with at least meningococcal immunotypes $L_2$ and $L_3$***" (claim 30, page 29).

Thus, Hoogerhout admitted that the existence of a cross-reactive epitope was merely a "possibility." In addition, had Hoogerhout known of the cross-reactive epitope of the subject application, Hoogerhout would not have stating that the cross-reactive conjugate reacts with both immunotypes L2 and L3, as quoted. Finally, the theoretical cross-reactive epitope of Hoogerhout can just as well be on the peptide (derived from the same organism as the OS) as on the OS, as indicated by the phrase: "the ***conjugate*** shows cross reaction." Thus, the quoted passages neither disclose nor suggest a cross-reactive epitope that is defined solely by the location of the PEA group on HepII, as recited in claims of the subject application.

The Examiner further alleged that Hoogerhout disclosed an LPS epitope containing one or more PEA groups and being derived from immunotype L3 (page 17, lines 2-4).

In response, Applicants respectfully assert that this disclosure neither discloses nor suggests the cross-reactive epitope recited in claims of the subject application. There is no suggestion in the quoted passages that an LPS epitope containing one or more PEA groups and being derived from immunotype L3 exhibits cross-reactivity with a plurality of *Neisseria* immunotypes.

The Examiner further alleged that Hoogerhout disclosed in Figure 2 a structure of immunotypes L1-L6.

In response, Applicants respectfully assert that this disclosure neither discloses nor suggests a cross-reactive epitope that is defined solely by the location of the PEA group on HepII, as recited in claims of the subject application. Which, if any, of the many conserved moieties depicted in Figure 2 forms a conserved epitope is left to the imagination.

The Examiner further alleged that Hoogerhout disclosed structures of "meningococcal inner core oligosaccharides comprising KDO, GlcNAc, HepI, HepII and one or more PEA linked to HepII at position 3 or 6/7 and a glucose."

In response, Applicants respectfully assert that this disclosure neither discloses nor suggests a cross-reactive epitope that is defined solely by the location of the PEA group on HepII, as recited in the new claims of the subject application. These structures contain multiple residues and do not indicate the importance of the position of the PEA group on HepII, thus in fact supporting Applicants' assertion.

Furthermore, Hoogerhout did not show that the antibody epitope recited in the claims of the subject application is useful for vaccination against each of a plurality of *Neisseria* immunotypes, as recited in new claims 55-61 of the subject application. Hoogerhout in fact completely lacked knowledge of the recited antibody epitope as described above. By contrast, the subject application showed that the recited epitope was present and accessible on 70% of a comprehensive set of invasive *Neisseria* lineages (page 33, first full paragraph). In addition, Hoogerhout provided no evidence that the antibodies elicited by the compositions are opsonically functional. By contrast, the subject application clearly demonstrates that antibodies elicited by the recited epitope are opsonically functional (opsonophagocytosis assay, pages 56-57). Thus, the subject application would provide a credible expectation to a person of average skill in the art that the presence of the recited epitope is sufficient to render a composition useful in vaccination against each of a plurality of *Neisseria* immunotypes; Hoogerhout, by contrast, would not provide this expectation. Thus, Hoogerhout neither disclosed nor suggested the subject matter of new claims 55-61 of the subject application.

The Examiner further alleged (paragraph bridging page 16 and page 17) that Hoogerhout disclosed that the PEA group was important in forming immunological epitopes and instructed "not to use the PEA group for coupling the *meningococcal* LPS oligosaccharide to a carrier peptide, but to retain the PEA group in the conjugate since the group forms a part of a number of immunotype-specific epitopes."

In response, this quotation actually supports Applicants' assertion that Hoogerhout did not disclose or suggest a cross-reactive epitope that is defined solely by the location of the PEA group on HepII, as recited in new claims of the subject application, since Hoogerhout

refers to "***immunotype-specific*** epitopes." By contrast, epitopes recited in claims of the subject application are cross-reactive across a plurality of immunotypes, as described above. Thus, these disclosures of Hoogerhout neither disclosed nor suggested the subject matter of new claims 55-61 of the subject application.

The Examiner further alleged (page 17, line 20- page 18, line 25) that Hoogerhout taught (a) that the saccharide part can be a fragment of the inner core region of the *meningococcal* LPS immunotype 6; (b) that *meningococcal* immunotypes L3 and L2 cause approximately from 70% to 30% of the group B *meningococcal* meningitis; (c) that the saccharide-peptide conjugate contains the saccharide and at least one T-helper cell activating part of *meningococcal* class I OMP and offers protection against *meningococci*; and (d) that the saccharide portion of the conjugate can be synthesized to obtain improved immunizing activity.

In response, Applicants respectfully assert that none of these findings disclosed or suggested a cross-reactive epitope that is defined solely by the location of the PEA group on HepII, as recited in claims of the subject application. Thus, these disclosures of Hoogerhout neither disclosed nor suggested the subject matter of new claims 55-61 of the subject application.

The Examiner further alleged (ibid) that "the property of reactivity with the B5 mAb is viewed as an inherent property inseparable from the immunogenic component of Hoogerhout."

In response, Applicants respectfully assert, as described above, that clearly had not knowledge of the cross-reactive epitope that is defined solely by the location of the PEA group on HepII, as recited in the claims of the subject application. Thus, this alleged inherent property of the compositions of Hoogerhout neither disclosed nor suggested the subject matter of new claims of the subject application.

In summary, Hoogerhout neither disclosed nor suggested that (a) the presence of PEA at position 3 of HepII of the *Neisserial* inner core LPS epitope is sufficient to define an antibody epitope present on a plurality of *Neisseria* immunotypes or (b) the antibody epitope recited in the claims of the subject application is useful for vaccination against each of a

plurality of *Neisseria* immunotypes. Therefore Hoogerhout neither disclosed nor suggested the subject matter of the new claims of the subject application.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejection.

In view of the foregoing amendments and remarks, the new set of claims is deemed to be allowable. Therefore, Applicants earnestly request consideration of new claims 48-61 under 37 C.F.R. § 1.114.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

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